

Supporting Information

The c-Abl Tyrosine Kinase Adopts Multiple Active Conformational States in Solution

John Badger, Prerna Grover, Haibin Shi, Shoghag B. Panjarian, John R. Engen, Thomas E. Smithgall, and Lee Makowski

Contents

Figure S1: Guinier plots

Figure S2: Particle distance distribution functions

Figure S3: Reconstruction of WT Abl protein with the small molecule compound, DPH

Figure S4: Replicated reconstruction of the molecular envelope of the Abl T315I mutant

Figure S1: Guinier plots

(A-F) show Guinier plots for each of the six related data sets measured in run 1. The values for R_g derived from linear fits to these plots lie in rank order: HAL9 (26.9 Å), HAL9+A365N (27.3 Å), HAL9+T315I (28.6 Å), A356N (29.7 Å) and WT (29.7 Å), T315I (31.4 Å). This order is consistent with the distribution of R_g values calculated using GNOM and given in Table 1.

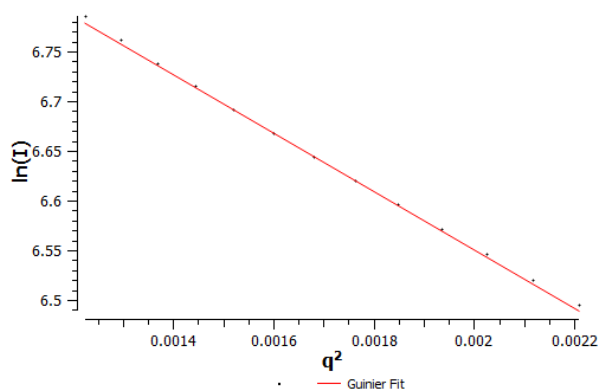
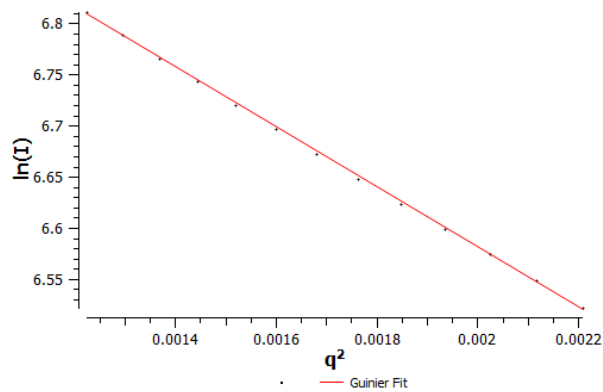
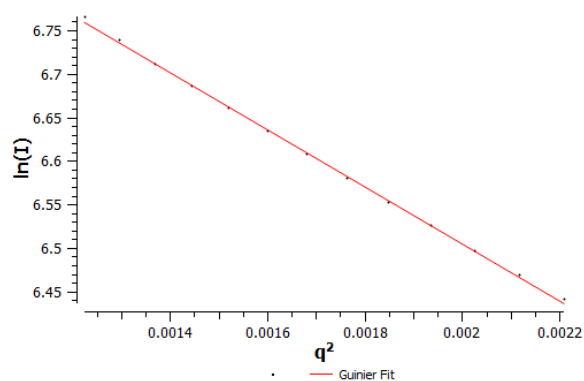
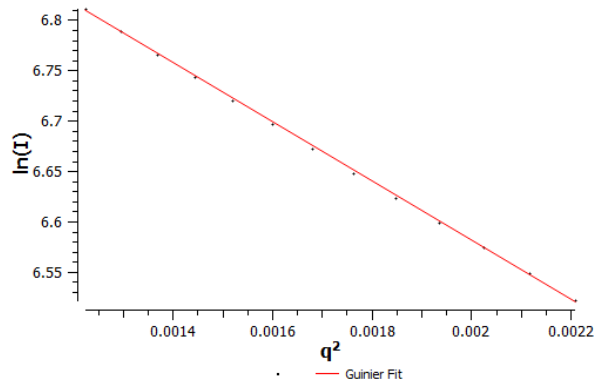
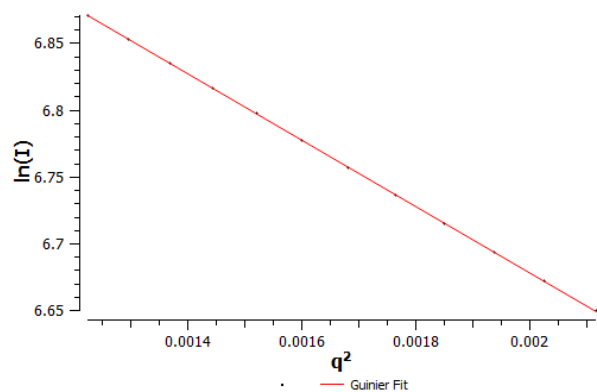
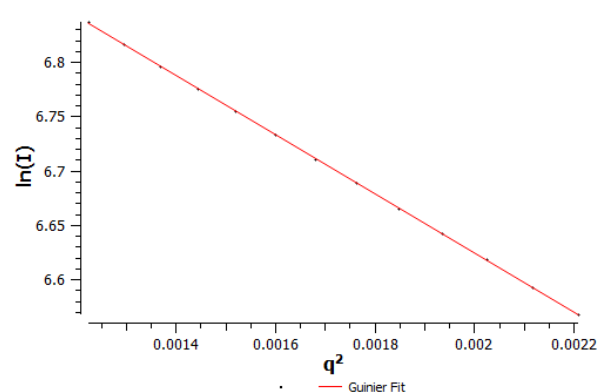
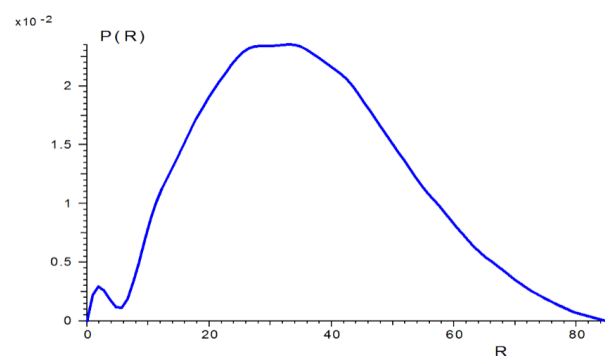
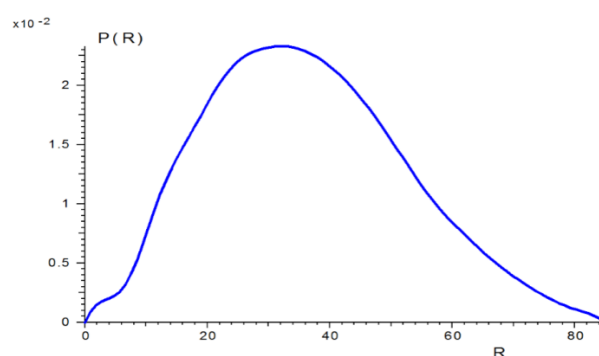
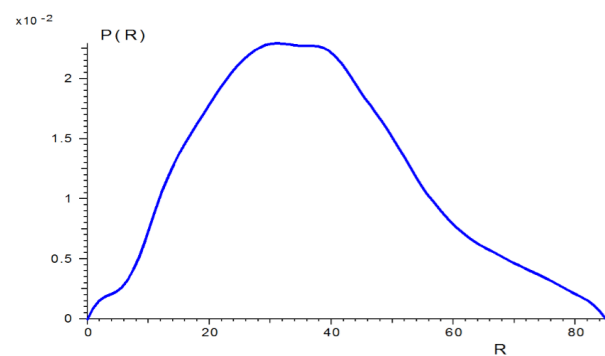
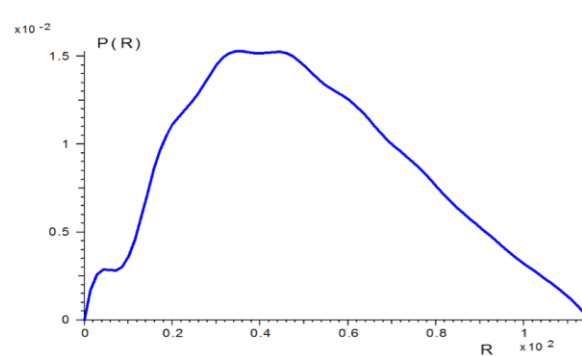
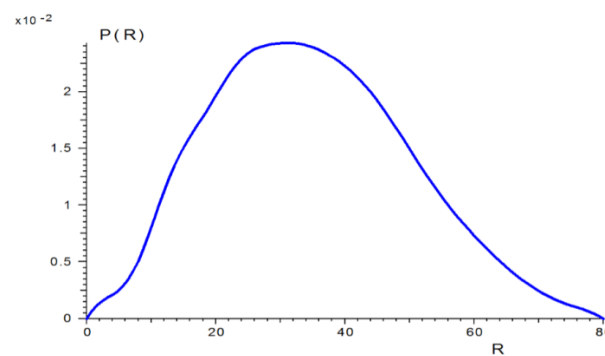
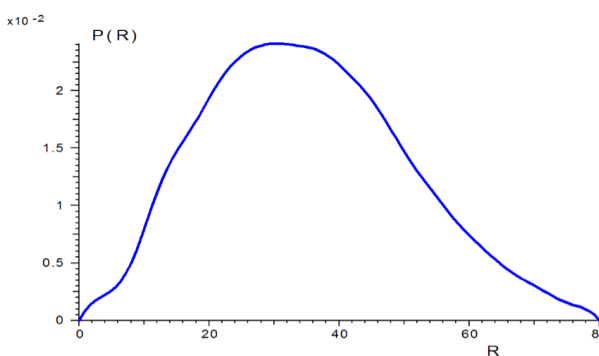
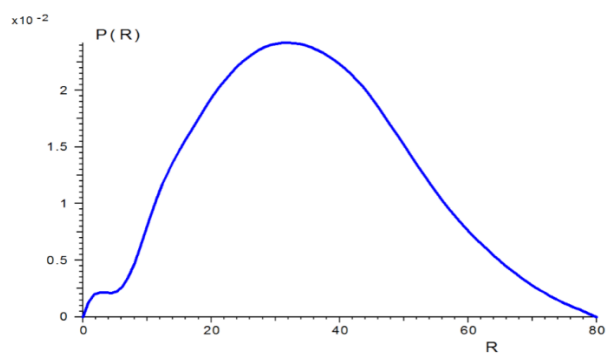
**(A) A356N****(B) WT****(C) T315I****(D) HAL9****(E) HAL9+A356N****(F) HAL9 + T315I**

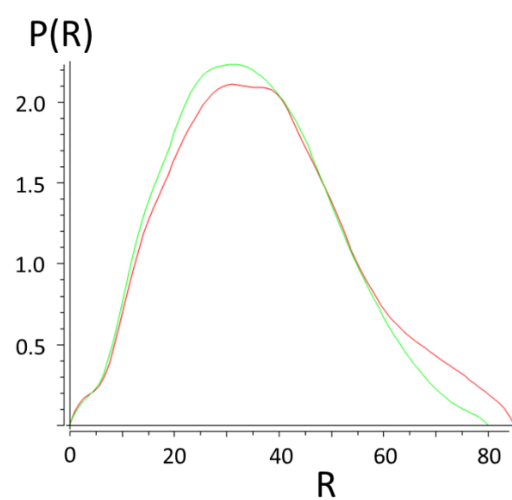
Figure S2: Particle distance distribution functions, $P(r)$

$P(r)$ is given as calculated from (A-C, E-G), the six data sets measured in run 1, and, (D) the $\Delta Ncap$ -PE data set measured in run 2. The particle distance distribution function for (D) $\Delta Ncap$ -PE, indicates a protein conformation with much greater extent than proteins in the other samples. Note that the $P(r)$ curve for (B) T315I has a somewhat different shape than the $P(r)$ curves for the remaining samples, which are relatively similar to each other. Plot (H) directly compares the $P(r)$ for the T315I mutant with the $P(r)$ for the HAL9 mutant.

**(A) A356N****(B) WT****(C) T315I****(D) $\Delta Ncap$ -PE****(E) HAL9****(F) HAL9+A356N**



(G) HAL9+T315I



(H) Overlay of $P(r)$ for the T315I mutant (red) and the HAL9 mutant (green).

Figure S3: Reconstruction of WT protein with the small molecule compound, DPH

Orthogonal views of the reconstructions of WT Abl protein combined with a 2-fold excess of the small molecule compound DPH [5-(1,3-diaryl-1H-pyrazol-4-yl)hydantoin)]. Supplementary data collected for this reconstruction extended over $0.035 < q < 0.79 \text{ \AA}^{-1}$, the $P(r)$ was calculated with $R_{\text{max}} = 85 \text{ \AA}$ and the reconstructed volume was obtained from the average of 10 reconstruction trials (clustering score, NSD = 1.07) using calculation methods described in the main text.

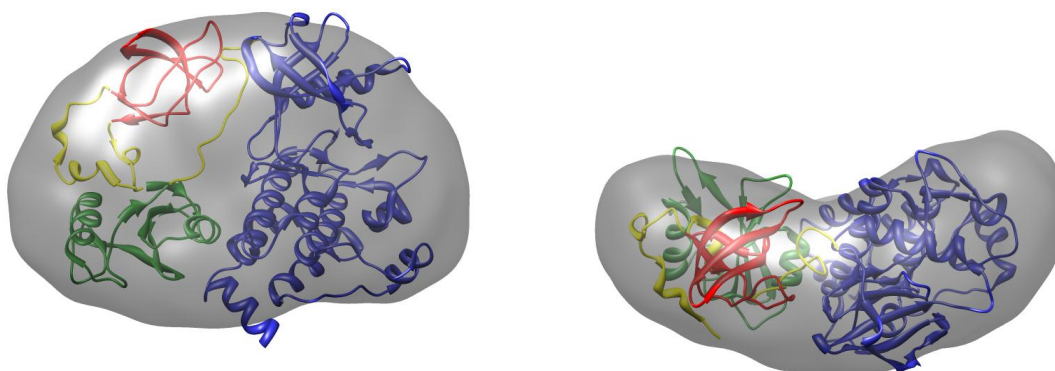


Figure S4: Replicated reconstruction of the molecular envelope of the Abl T315I mutant

Orthogonal views of the reconstructions of the Abl T315I mutant that were obtained from data collected in run 1 and the reconstruction obtained from data collected in run 2. Both reconstructions from this mutant have a pear-shaped appearance that is distinct from the ellipsoidal shapes of the molecular envelopes obtained from the other comparable Abl samples.

